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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,438	04/11/2006	Christopher Wheeler	22862-004US1 / 67789-570	4024

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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
02/04/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/575,438	WHEELER ET AL.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,11,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,11,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/14/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed November 13, 2009 in response to the Office Action of May 14, 2009, is acknowledged and has been entered. Claims 1-3, 5-7, 11, 25, and 26 are currently pending and being examined. Claims 1 and 25 are amended. Claims 4, 8-10, and 12-24 are canceled.

New Rejection

(based on new considerations)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-3, 5-7, 11, 25, and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a glioma in a mammal, the method comprising: (a) administering at least one vaccination of dendritic cells ("DC") to said mammal suffering from a glioma, **wherein said DC are autologous and primed *ex vivo* with autologous glioma cells**; and (b) after glioma recurrence following (a), administering a regimen of chemotherapy to said mammal, wherein said regimen of chemotherapy includes the administration of at least one chemotherapeutic agent selected from the group consisting of temozolomide, procarbazine, vincristine, BCNU, CCNU, thalidomide, irinotecan, isotretinoin, imatinib, etoposide, and combinations thereof, does not reasonably provide enablement for said method

comprising *administering any DC, DC that are not primed, or that are primed with any unknown source*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification discloses administering dendritic cells (DC) to newly diagnosed glioblastoma multiforme (GBM) patients, wherein patients received three vaccines, two weeks apart of 10-40X10^6 autologous DC loaded with either HLA7 eluted peptides from

cultures tumor cells of 150 ug/ml autologous tumor freeze-thaw lysate, starting approximately fifteen weeks post-surgery. The specification points to Yu et al (Cancer Research, 2001, 61:842-847, IDS) in Example 4, p. 17, to describe how blood was collected and vaccinations were administered. Yu et al teach that GBM patients' peripheral blood stem cells were collected and expanded *ex vivo* into DCs and pulsed with peptides eluted from the surface of cultured autologous brain tumor cells (p. 842, col. 1). The specification discloses that GBM patients receiving chemotherapy after vaccination with DC exhibited significantly prolonged survival relative to those receiving either treatment individually (Example 2; p. 13).

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide guidance or examples for treating glioma in patients comprising administering **DCs that are not primed**. The specification discloses only treatment of glioma by administration of DCs primed *ex vivo* with autologous tumor cells. The art teaches that unprimed or unpulsed DCs are ineffective for treating tumors. Okada et al (Int J Cancer, 1998, 78:196-201) teach that non-peptide-pulsed DCs failed to protect mice from brain tumor challenge (Figure 1 and 2). Liau et al (J Neurosurgery, 1999, 90:1115-1124) teach that rats with intracranial 9L gliomas treated with unpulsed DCs had a significantly shorter survival time than rats treated with tumor antigen-pulsed DCs, and the survival time for rats treated with unpulsed DCs was the same as that of rats treated with control media (p. 1118, col. 1-2; Figure 4). Heimberger et al (J of Neuroimmunology, 2000, 103:16-25) teach that vaccination with unpulsed DCs did not protect mice against glioma challenge and had

the same effect as phosphate-buffered saline, where as DCs pulsed or primed with glioma tumor protected mice against intracerebral challenge glioma cells (p. 20, col. 1; Figure 2). Given the teaching of the art, one of skill in the art could not predictably treat glioma in a mammal comprising administering any DCs that are not primed because they fail to initiate an immune response that can treat.

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide guidance or examples for treating glioma in patients comprising administering **DCs that are primed *ex vivo* with any unknown antigen or source**. The claims as currently constituted recite "wherein said DC are primed *ex vivo*." The art teaches that DCs must be primed with antigens expressed on the tumor being treated in order to be effective. Okada et al (above) teach that DCs pulsed with control peptides (control influenza peptides, "I-DC"), or peptides not expressed on the tumor, failed to protect mice from tumor challenge (Figure 1 and 2), whereas DCs pulsed with antigen expressed on the tumor (E7) were able to protect mice from tumor challenge. Zhang et al (Clinical Cancer Research, 2007, 13:566-575) teach that there are numerous and highly variable expression of tumor associated antigens on gliomas (p. 566, col. 2 to p. 567, col. 1; Table 2 and 3). Zhang et al teach that effective immunotherapy requires that the patients' neoplasm displays the tumor antigen properly associated with their restricted HLA alleles. This allows T-cell clonal expansion after their recognition. Given the teaching of the art, one of skill in the art could not predictably treat glioma in a patient with DCs primed *ex vivo* with any

unknown antigen or source, other than primed with the patient's autologous glioma cells that express the antigens required to be targeted by the DCs.

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide guidance or examples for treating glioma in patients comprising **administering DCs derived from any source including allogeneic DCs.** The specification only discloses treatment of glioma comprising administering autologous DCs. In the art, Merrick et al (Cancer Immunol Immunother, 2008, 57:897-906) compare allogeneic versus autologous DCs for treating tumors and demonstrate that autologous DCs provide significantly better protection against tumors than "semi-allogeneic" DCs (Figure 3). Merrick et al determined that there were detrimental effects from allogeneic MHC antigen expression by peptide-pulsed DC on murine *in vivo* CTL and tumor protection, which was also seen in naive human T-cell priming *in vitro*. Merrick et al conclude that autologous DC are preferable not only for peptide-pulsed vaccination strategies, but also for *in vitro* priming and expansion of T-cells for subsequent therapeutic adoptive transfer. Merrick et al teach that allogeneic DC are suboptimal for peptide-pulsed vaccination strategies (p. 905, col. 1). Given the teaching of the art, one of skill in the art could not predictably treat glioma in a mammal comprising administering any DCs other than autologous DCs.

Therefore, in view of the state of the art, the quantity of experimentation necessary, the breadth of the claims, lack of guidance in the specification, and the absence of working examples for treating glioma with any DCs, DCs that are not

primed, or primed with any source, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

3. All other rejections recited in the Office Action mailed May 14, 2009 are hereby withdrawn in view of amendments and arguments. Examiner acknowledges the amendment to the specification to correct an obvious error as stated in the Yu declaration submitted under 37 CFR 1.132. Dr. Yu states that data in the specification demonstrates that the survival of vaccine + chemotherapy group was significantly greater relative to survival in the other two groups together, and greater than survival in the chemotherapy group alone or the vaccine group alone.

4. **Conclusion:** No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642